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(54) Title: MULTIPLE VIRUS REPLICON CULTURE SYSTEMS

(57) Abstract: Methods and compositions are provided for screening candidate antiviral agents using cells containing subgenomic viral replication systems such as replicons and minigenomes. The methods involve the simultaneous assay of more than one subgenomic viral replication system. Compositions useful for theses methods are also provided.

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Primary screening programs to discover and identify compounds with antiviral activity can be designed in a variety of ways. All programs, however, fall into one of two general approaches. In the targeted approach, one particular biochemical target is chosen and candidate antiviral compounds are screened for inhibition of that target. The target is often an enzyme or a receptor that is known or thought to be essential to the process of viral replication. The alternative approach is unbiased such that inhibitors of viral replication are sought without *a priori* concern for the target. This unbiased approach generally involves use of cell culture since, as obligate intracellular pathogens, viruses can only replicate within cells. Although cell-based screening has been used successfully throughout the drug-discovery field, it is problematic when screening for antivirals. This is because it requires inoculation of infectious virus onto the cells and the production of additional infectious progeny virus. In particular, handling such infectious material is not easily compatible with the high throughput process of screening large libraries of compounds.

Thus, there is a need for improved methods and compositions that are useful for screening and analyzing antiviral compounds. In particular, these methods and compositions should be useful for high-throughput antiviral screening. The invention described herein satisfies